The Amsterdam Cohort Studies on HIV infection: annual report 2013

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Introduction

The Amsterdam Cohort Studies (ACS) on HIV infection and AIDS were started shortly after the first cases of AIDS were diagnosed in the Netherlands. Since October 1984, men who have sex with men (MSM) have been enrolled in a prospective cohort study. A second cohort involving drug users (DU) was initiated in 1985. In 2013, the cohorts reached 29 years of follow-up. The initial aim of the ACS was to investigate the prevalence and incidence of HIV-1 infection and AIDS and their risk factors, the natural history and pathogenesis of HIV-1 infection, and the effects of interventions. During the past 29 years, these aims have remained primarily the same, although the emphasis of the studies has changed. Early on, the primary focus was to elucidate the epidemiology of HIV-1 infection, whereas later more in-depth studies were performed to investigate the pathogenesis of HIV-1 infection. In recent years, the focus has shifted to also include the epidemiology and natural history of other blood-borne and sexually transmitted infections (STI) among the participants in the ACS.

From the beginning, research in the ACS has taken a multidisciplinary approach (epidemiology, social science, virology, immunology and clinical medicine). This unique collaboration has been very productive, significantly contributing to the knowledge and understanding of many different aspects of HIV-1 infection. This expertise has contributed directly to advances in prevention, diagnosis, and management of HIV infection.

As of 31 December 2013, 2,553 MSM and 1,661 injecting and non-injecting drug users were included in the ACS. Every three to six months, participants complete a standardised questionnaire designed to obtain information regarding medical history, sexual and drug use behaviour, underlying psychosocial determinants, healthcare use, depression, psychological disorders, and demographics. In addition, they undergo a medical examination (HIV-positive participants and, in the past, also HIV-negative drug users), and blood is collected for diagnostic tests and storage. The ACS have been conducted in accordance with the ethical principles set out in the declaration of Helsinki, and participation in the ACS is voluntary; written informed consent (the most recent version was approved by the AMC Medical Ethics

Committee in 2007 for the MSM cohort and in 2009 for the DU cohort) is obtained from each participant.

Of the 2,553 MSM, 604 were HIV-positive at entry into the study, and 240 seroconverted during follow-up. Of the 1,661 DU, 322 were HIV-positive at entry, and 99 seroconverted during follow-up. By 31 December 2013, 354 MSM and 538 DU had died, and several other participants were asked to leave the study or left at their own request. In total, the Public Health Service of Amsterdam was visited 53,466 times by MSM and 27,409 times by DU.

Collaborating institutes and funding

Within the ACS, different institutes collaborate to bring together the data and biological sample collections and to conduct research. These include the Public Health Service of Amsterdam (PHSA) (Infectious Diseases Cluster, Department of Research), the Academic Medical Center (AMC) of the University of Amsterdam (Departments of Medical Microbiology, Experimental Immunology, Internal Medicine, Division of Infectious Diseases, (HIV treatment centre, Emma Kinderziekenhuis), University Medical Center Utrecht (UMCU, Department of Immunology), Stichting HIV Monitoring (SHM), the Jan van Goyen Medical Centre (Department of Internal Medicine) and the HIV Focus Centre (DC Klinieken) Amsterdam. From the start, Sanquin Blood Supply Foundation has been involved in the ACS and, until 2007, research in the ACS was conducted by the Department of Clinical Viro-Immunology at Sanquin Research. Sanquin financially supports the maintenance of the biobank of viable peripheral blood mononuclear cells at the Department of Experimental Immunology at the AMC. In addition, there are numerous collaborations between the ACS and other research groups both within and outside of the Netherlands. The ACS is financially supported by the Centre for Infectious Disease Control of the Netherlands National Institute for Public Health and the Environment (*Rijksinstituut voor Volksgezondheid en Milieu,* RIVM).

The ACS in 2013

Scientific evaluation

An international Scientific Evaluation Committee (SEC), led by Chairman Prof. A. Hofman of Erasmus University Medical Center (Erasmus MC) in Rotterdam, visited Amsterdam on 23 January 2013 to review the ACS. This review was requested by the main funder of the Amsterdam Cohort Studies, the RIVM. Both the scientific achievements of the past five years and the scientific plans for the future were examined.

In February, the SEC sent its evaluation, which was a strong endorsement of the ACS. The major conclusions were: 1. The scientific output is both quantitatively and qualitatively high; 2. The ACS is a unique and internationally very important prospective cohort study, particularly because of its emphasis on HIV-negative participants and long-term follow-up; 3. The research issues of the ACS are well positioned to answer major questions and make important contributions. The SEC recommended the continued funding of the ACS. Following this positive evaluation, the RIVM decided to continue funding the ACS. Based on research plans and the state of the epidemic in the Netherlands, the ACS project leaders proposed that the group of HIV-negative MSM should be expanded during the next few years and that follow-up of the group of DU should be reduced. The SEC agreed to these suggestions, and implementation of these changes was initiated in January 2014.

The cohort of men having sex with men

In 2013, 664 MSM were in active follow-up within the ACS. Of the MSM in active follow-up by the end of 2013, 543 were HIV-negative, and 121 were HIV-positive. The median age of the MSM was 40.9 years (interquartile range (IQR) 35.7-46.2), 7.4% were non-Dutch, and 80.0% had attained a high level of education. The majority of the participants (85%) were residents of Amsterdam. Fifty-three participants were newly recruited, and two died in 2013.
Until 1995, men of all age groups were eligible to participate if they lived in or around Amsterdam and had had at least two male sexual partners in the previous six months. During the period 1995–2004, only men aged ≤30 years with at least one male sexual partner in the previous six months could enter the study. Since 2005, recruitment has been open to MSM of all ages with at least one sexual partner in the preceding six months.
In 1999, follow-up of HIV-positive participants was transferred from the PHSA to the Jan van Goyen Medical Centre in Amsterdam, and six-monthly behavioural follow-up ceased. However, since 2000, HIV-infected MSM in follow-up at the Jan van Goyen Medical Centre have again been asked to complete behavioural ACS questionnaires once a year.
In 2013, 176 of the HIV-positive MSM were in active follow-up at the Jan van Goyen Medical Centre or, as of October 2013, at the HIV Focus Centre. Of these 176 participants, 43 were HIV seroconverters, and 33 were defined as slow or non-progressors or matched fast progressors in 1996 or were HIV-positive for more than 10 years and had a CD4 count greater than 400 cells/mm^3 after 10 years of HIV-positive follow-up without antiretroviral therapy. In total, 39 MSM in active follow-up at the Jan van Goyen Medical Centre completed the behavioural questionnaire.
Behavioural and clinical follow-up of individuals with a recent HIV infection at study entry at the PHSA and of HIV seroconverters during the period after 1999 was initiated in October

2003 in accordance with the 'HIV Onderzoek onder Positieven' (HOP) protocol (*HIV Research in Positive Individuals*). These participants return for follow-up at the PHSA or at an HIV treatment centre. All ACS behavioural data are collected on a six-monthly basis, and clinical data are provided by SHM. Of the 83 HIV-positive MSM in active follow-up in 2013 in accordance with the HOP protocol, 13 were newly included, and 55 were HIV seroconverters. A behavioural questionnaire was completed by 80 HIV-positive MSM as part of the HOP protocol.
In 2006, HIV-positive steady partners of HIV-negative participants and all steady partners of HIV-positive participants were also invited to participate in the ACS. Thirteen HIV discordant and 3 HIV-positive concordant couples were included in this partner study, of which 3 couples were still in active follow-up in 2013.
Since November 2008, all MSM followed at the PHSA have been routinely screened for STI.

The cohort of drug users

In 2013, 252 DU were followed at the PHSA. The median age of the DU was 51.7 years (IQR 44.9-56.5), 15.9% were non-Dutch, and 8.7% had attained a high level of education. Two hundred and thirty-eight (94.4%) were residents of Amsterdam. Of the 252 DU followed in 2013, 16 were HIV-positive at entry, 12 seroconverted for HIV during follow-up in the ACS. Since July 2009, individuals between 18 and 30 years who regularly use hard drugs in Amsterdam and individuals older than 30 years who have started injecting hard drugs in the preceding two years in Amsterdam have been eligible for inclusion in the ACS. No new participants were recruited in 2013, which might be because injecting drug use has become less common in Amsterdam.

The Drug Users Treatment for Chronic Hepatitis-C (Dutch-C) study was started in 2005 within the DU cohort to evaluate the possibility of HCV testing and treatment combined with methadone programmes. This project aimed to offer HCV screening and treatment to all DU participating in the ACS and to develop guidelines for HCV treatment of active DU outside a clinical setting. Drug users were offered HCV testing and, if chronically infected, medical and psychiatric screening and HCV treatment. Various specialists collaborated to provide optimal HCV care at the PHSA. The first active DU chronically infected with HCV genotype 1 started treatment with telaprevir combined with pegylated interferon and ribavirin at the PHSA in 2012. In collaboration with the AMC, treatment of HCV-infected DU at the PHSA continued in 2013.

Subgroup studies and affiliated studies

AGE_hiV Cohort Study

The AGE_hiV Cohort Study, a collaboration between the AMC Department of Infectious Diseases, Department of Global Health, and Amsterdam Institute of Global Health and Development, the PHSA, and SHM, was started in October 2010. The aim of the study is to assess the prevalence and incidence of a broad range of co-morbidities and known risk factors for these co-morbidities in HIV-infected patients aged ≥45 years and to determine the extent to which co-morbidities, their risk factors and their relation to quality of life differ between HIV-infected and uninfected groups. Participants undergo a comprehensive assessment for co-morbidities and fill in a questionnaire at intake and 2 years afterwards. In total, 598 HIV-1-infected participants and 550 HIV-uninfected individuals completed a baseline visit between October 2010 and September 2012. HIV-1-infected participants were included through the AMC HIV outpatient clinic and HIV-uninfected participants from the same HIV exposure groups were included through the STI clinic of the PHSA (n=486) or the ACS (n=64). All participants were aged ≥45 years and were as comparable as possible with respect to age, gender, ethnicity, and risk behaviour. By the end of 2013, the second data wave was still ongoing, and 402 HIV-1-infected participants and 319 HIV-uninfected individuals had returned for their second visit.

ACS biobank

The ACS visits, together with data collection from several subgroup studies and affiliated studies, have resulted in a large collection of stored samples.

The ACS biobank includes plasma and peripheral blood mononuclear cell samples collected within the context of the Primo-SHM study (a national randomised study on the effects of early temporary antiviral therapy as compared to no therapy among patients who presented with primary HIV-1 infection at the AMC outpatient clinic and ACS seroconverters). These samples are stored at the AMC. At present, the biological samples are still being collected prospectively for Primo-SHM participants visiting the AMC clinic until one year after they have recommenced therapy.

The ACS biobank also includes plasma and peripheral mononuclear cell samples that were collected from both HIV-infected and HIV-exposed children at the Emma Kinderziekenhuis in the AMC until 2008. These are also stored at the AMC. Currently, no new samples are being collected within the ACS setting.

All stored samples are available for ACS research.

The HIV epidemic

HIV incidence

Two MSM and no DU participating in the ACS seroconverted for HIV in 2013. The observed HIV incidence among MSM declined to 0.39 per 100 person years in 2013.

The HIV incidence in drug users has been stable since 2008, with less than one case per 100 person years. *Figures 9.1* and *9.2* show the yearly observed HIV incidence rates for MSM and DU from the start of the ACS through 2013.

Figure 9.1: *HIV incidence per calendar year in the Amsterdam Cohort Studies (ACS) among men who have sex with men (MSM), 1984-2013.*

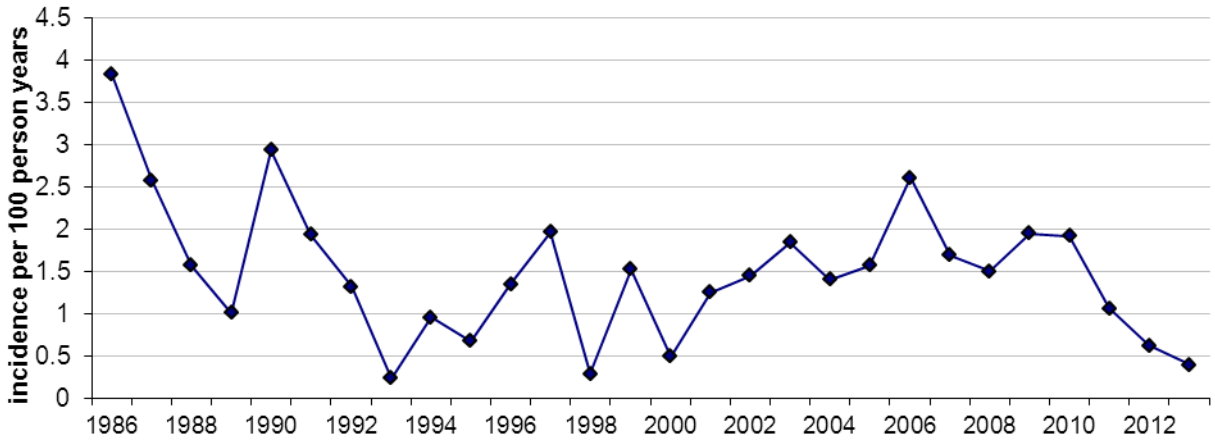
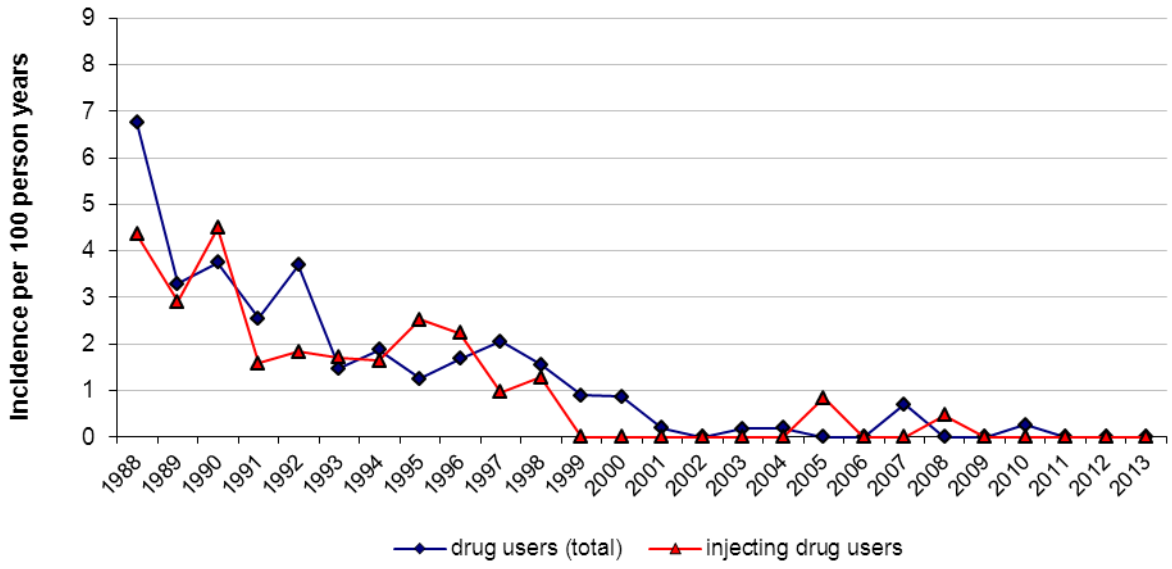


Figure 9.2: *HIV incidence per calendar year in the Amsterdam Cohort Studies (ACS) among drug users, 1986-2013.*



Transmission of therapy-resistant HIV strains

In 2013, surveillance of transmission of drug-resistant HIV-1 strains was performed for four MSM seroconverters who had their first visit after being found to be HIV-positive in 2013 (two of them had an estimated seroconversion moment in 2012) and for five MSM who were seropositive at study entry. One of these five MSM experienced an acute HIV-1 infection at study entry. One of the seroconverters was infected with a virus harbouring a so-called 215-revertant (215S) mutation in the reverse transcriptase gene. In all individuals, naturally occurring sequence variation was found in the protease gene. Phylogenetic analysis showed a variety of HIV-1 subtypes: six individuals harboured subtype B HIV-1 strains; one had subtype A1; one had subtype F1; and one had subtype G.

In the cohort of drug users, there were no seroconversions or seropositive entries.

Highly active antiretroviral therapy (HAART) uptake

Of all 210 HIV-positive MSM from the ACS visiting the Jan van Goyen Medical Centre or one of the other HIV treatment centres in the Netherlands in 2013 and for whom treatment data were available, 206 (98%) received some form of antiretroviral therapy. Of 206 MSM for whom viral load results were available in 2013, 194 (94%) had a viral load of <50 copies/ml (assays M2000rt). Of the 27 HIV-positive DU who visited the PHSA in 2013 and for whom

treatment data were available, 26 (96%) received some combination of antiretroviral therapy. Of the 27 DU, 25 (93%) had an undetectable viral load (≤150 copies/ml [assay: M2000rt]) at their latest visit.

HPV in MSM

The H2M (HIV and HPV in MSM) study is a successful collaboration between the Centre for Infectious Disease Control (CIb), PHSA, the Jan van Goyen Medical Centre, VU University Medical Center (VUmc), and the AMC. The study aims to compare the prevalence, incidence, and clearance of high-risk (hr) human papillomavirus (HPV) infections between HIV-negative and HIV-infected MSM.

The participants were recruited from three sites: the ACS (n=520; mostly HIV-negative), the PHSA STI clinic (n=120; all HIV-infected), and the Jan van Goyen Medical Centre (n=160; all HIV-infected). Recruitment was carried out in 2010 and 2011, and participants were followed for 24 months. Participants provided self-collected swabs from the anus and penile shaft, as well as oral rinse-and-gargle specimens. These were tested for the presence of HPV DNA and, if positive, HPV types were determined. Serum was tested for L1 HPV antibodies.

The study found that hrHPV infections are more common in HIV-infected than in HIV-uninfected men. This was true for oral, penile, and anal infections. For example, HPV-16 was found in the anus of 22% of HIV-infected men and in 13% of HIV-uninfected men. HIV-infected men were also significantly more often seropositive for hrHPV types. In this cohort, anal infections were much more strongly associated with seropositivity than penile infections.

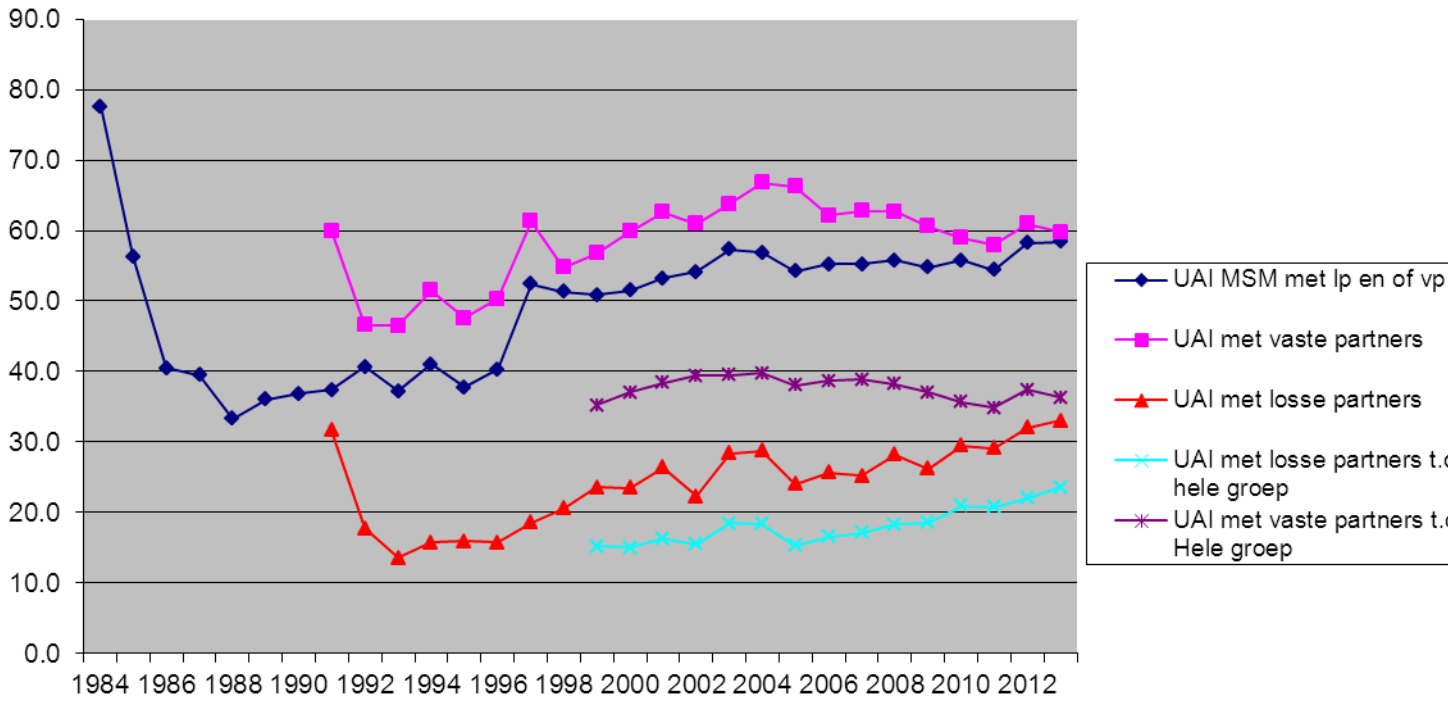
It is known that HPV vaccines induce high antibody concentrations and that vaccination prevents infection and re-infection (presumably through high antibody titres). The H2M study showed that concentrations observed after natural infection were much lower than those induced by vaccines. Importantly, in this cohort the presence of these natural antibodies was not protective against subsequent infections.

Analyses of the incidence of hrHPV infections over the two-year follow-up period are underway.

Risk behaviour of MSM

Information from the questionnaires completed by 545 HIV-negative MSM during cohort visits in 2013 resulted in 295 (54%) reports of unprotected anal intercourse (UAI) in the preceding six months. Higher proportions of UAI were reported for steady partners (60%) compared to casual partners (33%). Trends in UAI among HIV-negative MSM who are participants in the ACS, especially those with casual partners, continue to show a slow increase from 1996 onwards. (*Figure 9.3*).

Figure 9.3: *Trends shown by the Amsterdam Cohort Studies (ACS) in unprotected anal intercourse (UAI) in the past six months among HIV-negative men having sex with men (MSM) with a casual and/or steady partner, 1984-2013.*

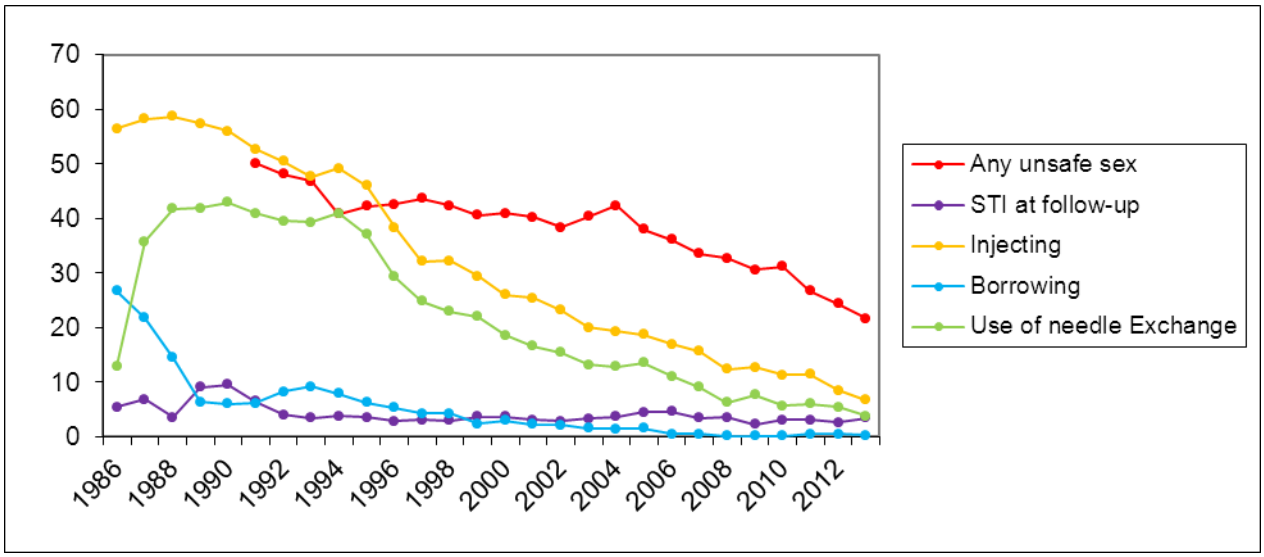


Risk behaviour of DU

In HIV-negative DU, reports of both injection and borrowing needles significantly declined over the period 1985-2013. Reports of high-risk sexual behaviour at follow-up visits decreased before 1996, then remained relatively stable until 2005, and further decreased to

approximately 22% in 2013. Reports of STI have remained relatively stable at approximately 3% in recent years (see *Figure 9.4*).

Figure 9.4: *Proportion of visits per calendar year at which injecting and high-risk sexual behaviour was reported amongst 1,339 drug users (DU) who were HIV-negative on entry to the Amsterdam Cohort Studies (ACS), 1986-2013.*



Legend: *STI = sexually-transmitted infection*

STI screening among MSM in ACS

Since October 2008, all MSM in the ACS have been routinely screened for chlamydia and gonorrhoea by polymerase chain reaction (PCR) techniques using urine samples and pharyngeal and rectal swabs. Cases of syphilis are detected by *Treponema pallidum* haemagglutination assay (TPHA). In 2013, a total of 604 MSM from the ACS were screened for STI. The overall prevalence of any STI was 5.9% (66/1,110).

ACS 2013 research highlights

The emergence of HIV variants (X4-HIV) that use chemokine receptor 4 (CXCR4) is associated with accelerated disease progression in the absence of antiretroviral therapy. However, the effect of X4-HIV variants on the treatment response remains unclear. In a recent study, we observed that patients harbouring X4-HIV variants prior to the start of treatment show a delay in time to viral suppression below the viral load detection limit. This delay in viral suppression was independently associated with high viral load and the

presence of X4-HIV variants. Furthermore, absolute CD4+ T cell counts were significantly lower in patients harbouring X4-HIV variants at all time points during follow-up. However, no differences were observed in the increase in absolute CD4+ T-cell numbers after treatment initiation, indicating that the reconstitution of CD4+ T cells is independent of the presence of X4-HIV variants. The emergence of X4-HIV has been associated with an accelerated CD4+ T cell decline during the natural course of infection and, therefore, patients in whom X4-HIV variants develop may benefit from earlier treatment initiation to achieve faster reconstitution of the CD4+ T cell population to normal levels (*245*).

Current HIV-1 envelope glycoprotein (Env) vaccines are unable to induce cross-reactive neutralising antibodies. Such antibodies are elicited in 10% to 30% of HIV-1 infected individuals, but it is unknown why these antibodies are induced in some individuals and not in others. We hypothesised that the Envs of early HIV-1 variants in individuals who have cross-reactive neutralising activity (CrNA) might also have unique characteristics that support the induction of CrNA. We retrospectively generated and analysed env sequences of early HIV-1 clonal variants from 31 individuals with diverse levels of CrNA two to four years after seroconversion. These sequences revealed a number of Env signatures that coincided with CrNA development, including a statistically shorter variable region 1 and a lower probability of glycosylation, as implied by a high ratio of NXS versus NXT glycosylation motifs. Furthermore, the lower probability of glycosylation at position 332, which is involved in the epitopes of many broadly reactive neutralising antibodies, was associated with the induction of CrNA. Finally, Sequence Harmony identified a number of amino acid changes associated with the development of CrNA. These residues mapped to various Env subdomains, but, in particular, to the first and fourth variable region as well as the underlying α2 helix of the third constant region. These findings imply that the development of CrNA might depend on specific characteristics of early Env. Env signatures that correlate with the induction of CrNA might be relevant for the design of effective HIV-1 vaccines (*246*).

The largest population of people at risk for HCV infection is injecting drug users (IDU). We hypothesise that recurrent exposure to HCV by continuing risk behaviour influences the development of an HCV-specific T-cell response. Therefore, we studied the association between repeated exposure to HCV and the height and focus of the HCV-specific T-cell response in HCV antibody-positive injecting DU (n=18) with ongoing risk behaviour ('high risk'), nine with and nine without detectable HCV RNA), and nine never-injecting DU ('low

risk', HCV RNA+). Both total HCV-specific T-cell response and the T-cell response against HCV non-structural proteins were significantly higher in IDU compared to never-injecting DU. Interestingly, the high-risk HCV RNA-negative group had no measurable CD4(+) T-cell response to HCV Core protein, compared to detectable responses to Core in the HCV RNA+ group. Thus, both ongoing risk behaviour and presence of HCV RNA affect the HCV-specific T-cell response in both magnitude and specificity, which may have implications for vaccine development (*247*).

Individuals with HIV infection are frequently also infected with hepatitis C virus (HCV) (co-infection), but little is known about its effects on progression of HIV-associated disease. In this study we determined the effects of HCV co-infection on mortality not only from HIV and/or AIDS but also from hepatitis- or liver-related, natural, and non-natural mortality. Data were used from the CASCADE cohort, which is a database of patients with well-established dates of HIV infection from Europe, Australia, and Canada. The ACS contribute data from HIV seroconverters among MSM and DU. Of 9,164 individuals with HIV infection, 2,015 (22.0%) were also infected with HCV. Among individuals infected with only HIV or with co-infection, the mortality from HIV infection and/or AIDS-related causes and hepatitis or liver disease decreased significantly after 1997, when combination antiretroviral therapy (cART) became widely available. However, after 1997, HIV and/or AIDS-related mortality was higher among co-infected individuals than those with only HIV infection. Compared to individuals infected with only HIV, co-infected individuals had a higher risk of death from hepatitis or liver disease. This underscores the importance of early diagnosis of HCV infection in HIV-infected individuals and the need for routine screening of HCV among high-risk groups. The authors conclude that it is necessary to evaluate the effects of HCV therapy on HIV progression (*248*).

Hepatitis B virus (HBV) is divided into eight definite (A-H) and two putative (I, J) genotypes that show a geographical distribution. HBV genotype G, however, is an aberrant genotype of unknown origin that demonstrates severe replication deficiencies and very little genetic variation. HBV-G infections are mainly noticeable after infection with a “helper” HBV strain, and especially during HIV-1 co-infection that decreases HBV immune control and increases HBV replication. There are indications that mixed HBV infections that include an HBV-G strain are associated with increased liver fibrosis, suggesting that patients infected with HBV-G should be monitored more closely. At the Academic Medical Center, the prevalence of HBV-G was determined in 96 HBV-infected patients with a newly developed real-time PCR assay that detects HBV-A and HBV-G. Ten HBV-G infections were detected exclusively in

HIV-1 infected men as co-infection with HBV-A. These findings suggest a strong association of HBV-G in the Netherlands with the HIV-1 infected male risk group, as has been reported from other countries (*249*).

Steering committee: 'The politburo'

In 2013, the politburo met four times. Twenty proposals for use of data and/or samples (serum/PBMC) were submitted to the politburo: three from the AMC Experimental Immunology department, six from the AMC Medical Microbiology department, six from the UMCU, four from the PHSA, and one from the AMC internal medicine division. Seventeen requests were approved, some after revision, and three requests were denied. Three of the approved proposals were collaborations with groups abroad (outside the ACS).

Publications in 2013 that include ACS data

1. de Vos AS, van der Helm JJ, Matser A, Prins M, Kretzschmar ME. **Decline in incidence of HIV and Hepatitis C virus infection among injecting drug users in Amsterdam; evidence for harm reduction?** *Addiction 2013 Jun;108(6):1070-81.*
2. Euler Z, van Gils MJ, Boeser-Nunnink BD, Schuitemaker H, van Manen D. **Genome-wide association study on the development of cross-reactive neutralizing antibodies in HIV-1 infected individuals.** *PLoS One 2013;8(1):e54684.*
3. Gijsbers EF, van Sighem A, Harskamp AM, Welkers MR, de Wolf F, Brinkman K, Prins JM, Schuitemaker H, van 't Wout AB, Kootstra NA. **The presence of CXCR4-using HIV-1 prior to start of antiretroviral therapy is an independent predictor of delayed viral suppression.** *PLoS One 2013 Oct 1;8(10):e76255*.
4. Gijsbers EF, Feenstra KA, van Nuenen AC, Navis M, Heringa J, Schuitemaker H, Kootstra NA. **HIV-1 replication fitness of HLA-B*57/58:01 CTL escape variants is restored by the accumulation of compensatory mutations in gag.** *PLoS One 2013 Dec 5;8(12):e81235.*
5. Grady BP, Schinkel J, Thomas XV, Dalgard O. **Hepatitis C virus reinfection following treatment among people who use drugs.** *CID 2013 Aug 15;57(suppl.2):S105-S110.*
6. Grebely J, Page K, Sacks-Davis R, Schim van der Loeff M, Rice TM, Bruneau J, Morris MD, Hajarizadeh B, Amin J, Cox AL, Kim AY, McGovern BH, Schinkel J, George J, Shoukry NH, Lauer GM, Maher L, Lloyd AR, Hellard M, Dore GJ, Prins M; the InC3 Study Group. **The effects of female sex, viral genotype, and IL28B genotype on spontaneous clearance of acute hepatitis C Virus infection.** *Hepatology 2013 Aug 2 [Epub ahead of print].*

7. Grebely J, Morris MD, Rice TM, Bruneau J, Cox AL, Kim AY, McGovern BH, Shoukry NH, Lauer G, Maher L, Lloyd AR, Hellard M, Prins M, Dore GJ, Page K; InC Study Group. Cohort Profile: **The International Collaboration of Incident HIV and Hepatitis C in Injecting Cohorts (InC3) Study.** *Int J Epidemiol 2013 Dec;42(6):1649-59.*
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9. Jazaeri Farsani SM, Jebbink MF, Deijs M, Canuti M, van Dort KA, Bakker M, Grady BP, Prins M, van Hemert FJ, Kootstra NA, van der Hoek L. **Identification of a new genotype of Torque Teno Mini virus.** *Virol J 2013 Oct 30;10:323.*
10. Lambers FAE, Prins M, Davidovich U, Stolte IG. **High awareness of hepatitis C virus (HCV) but limited knowledge of HCV complications among HIV-positive and HIV-negative men who have sex with men.** *AIDS Care 2014 Apr 26(4):416-24.*
11. Lodi S, del Amo J, d'Arminio Monforte A, Abgrall S, Sabin C, Morrison C, Furrer H, Muga R, Porter K, Girardi E; CASCADE collaboration in EuroCoord. **Risk of tuberculosis following HIV seroconversion in high-income countries.** *Thorax 2013 Mar;68(3):207-13.*
12. McLaren PJ, Coulonges C, Ripke S, van den Berg L, Buchbinder S, Carrington M, Cossarizza A, Dalmau J, Deeks SG, Delaneau O, De Luca A, Goedert JJ, Haas D, Herbeck JT, Kathiresan S, Kirk GD, Lambotte O, Luo M, Mallal S, van Manen D, Martinez-Picado J, Meyer L, Miro JM, Mullins JI, Obel N, O'Brien SJ, Pereyra F, Plummer FA, Poli G, Qi Y, Rucart P, Sandhu MS, Shea PR, Schuitemaker H, Theodorou I, Vannberg F, Veldink J, Walker BD, Weintrob A, Winkler CA, Wolinsky S, Telenti A, Goldstein DB, de Bakker PI, Zagury JF, Fellay J. **Association study of common genetic variants and HIV-1 acquisition in 6,300 infected cases and 7,200 controls.** *PLoS Pathog 2013;9(7) [Epub 2013 Jul 25].*
13. Madec Y, Boufassa F, Porter K, Prins M, Sabin C, Monforte AD, Amornkul P, Bartmeyer B, Sannes M, Venet A, Lambotte O, Meyer L; on behalf of the CASCADE Collaboration in Eurocoord. **Natural History of HIV control since seroconversion.** *AIDS 2013 Aug 1; 27:2451-60.*
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15. Mooij SH, Boot HJ, Speksnijder AG, Stolte IG, Meijer CJ, Snijders PJ, Verhagen DW, King AJ, Vries HJ, Quint WG, Sande MA, Loeff MF. **Oral human papillomavirus infection in**

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Theses in 2013 that include ACS data

Michel de Vries - January 29, 2013:Virus discovery and human parechoviruses. Supervisor: Prof. B. Berkhout; Co-supervisor : Dr. C.M. van der Hoek

Anouk Urbanus - March 21, 2013: Hepatitis C virus infection; spread and impact in the Netherlands. Supervisors: Prof. R.A. Coutinho and Prof. M. Prins.

Esther Gijsbers - July 4, 2013, HIV-1 evolution and adaptation to the host during the course of infection. Supervisor: Prof. H. Schuitemaker; co-supervisor: Dr. N.A. Kootstra